IN THE CLAIMS

Please amend the claims as follows:

1. (Currently Amended) A method to identify one or more agents with dual therapeutic activity, comprising:

a) selecting one or more agents which inhibit ~~or treat one or more symptoms of a disease which is associated with aberrant~~ expression or activity of amiloride-sensitive epithelial sodium channels (ENaC) having α, β and γ subunits of ENaC;

b) contacting *in vitro* mammalian cells with the one or more agents and a viral gene therapy vector; and

c) identifying an agent from those contacted with the mammalian cells that enhances the transduction ~~efficacy~~ of the viral gene therapy vector relative to mammalian cells contacted with the viral gene therapy vector but not contacted with the one or more agents.

2. (Currently Amended) A method to identify one or more agents with dual therapeutic activity, comprising:

a) selecting one or more agents that enhance the transduction ~~efficacy~~ of a viral gene therapy vector in mammalian cells;

b) contacting *in vitro* mammalian cells having aberrant expression or activity of amiloride-sensitive epithelial sodium channels (ENaC) having α, β and γ subunits of ENaC with the one or more agents; and

c) identifying an agent from those contacted with the mammalian cells that alters ENaC expression or activity.

3. (Canceled)

4. (Currently Amended) The method of claim 1 or 2 [[3]] wherein the viral vector is a retroviral vector, a lentiviral vector, an adenoviral vector of an adeno-associated viral vector.

5. (Original) The method of claim 1 wherein the gene therapy vector comprises a marker gene.

6. (Original) The method of claim 2 wherein the mammalian cells do not express functional CFTR.

7. (Original) The method of claim 2 wherein the selected agent is effective to decrease the level or amount of transcription of one or more subunits of ENaC.

8. (Withdrawn) The method of claim 2 wherein the selected agent is effective to decrease the level or amount of transcription of the α, β and γ subunits of ENaC.

9. (Withdrawn) The method of claim 2 wherein the selected agent is effective to alter ENaC activity.

10. (Withdrawn) A method to identify one or more agents that decrease the level or amount of transcription of one or more subunits of epithelial sodium channels (ENaC) in mammalian cells, comprising:

a) contacting mammalian cells which express ENaC with at least one agent that is a proteasome modulating agent, wherein the agent is not a gene or gene product encoded by the genome of the cells, the complement of the gene, or a portion of the gene or its complement; and

b) identifying whether an agent decreases the level or amount of transcription from one or more subunits of ENaC in the mammalian cells.

11. (Withdrawn) A method to identify one or more agents that decrease the level or amount of transcription from the α, β, and γ subunits of ENaC in mammalian cells, comprising:

a) contacting mammalian cells which express ENaC with at least one agent; and

b) identifying whether an agent decreases the level or amount of transcription from the α, β, and γ subunits of ENaC in the mammalian cells.

12. (Withdrawn) A method to identify one or more agents that decrease the level or amount of transcription of one or more subunits of ENaC in mammalian cells, comprising:

a) contacting mammalian cells which express ENaC with at least one agent that enhances viral transduction; and

b) identifying whether an agent decreases the level or amount of transcription from one or more subunits of ENaC in the mammalian cells.

13. (Currently Amended) The method of any one of claims 1 to 2 ~~or 10 to 12~~ wherein the cells are mammalian lung or kidney cells.

14. (Withdrawn) The method of claim 11 or 12 wherein the one agent is not a gene or gene product encoded by the genome of the cells, the complement of the gene, or a portion of the gene or its complement cells are mammalian kidney cells.

15. (Currently Amended) The method of any one of claims 1 to 2 ~~or 10 to 12~~ wherein the cells are human cells, canine cells, murine cells, rat cells or rabbit cells.

16. (Currently Amended) The method of any one of claims 1 to 2 ~~or 10 to 12~~ wherein one of the agents is an antibiotic.

17. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is a chemotherapeutic.

18. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is a lipid lowering agent.

19. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is a food additive.

20. (Currently Amended) The method of any one of claims 1 to 2 ~~or 10 to 12~~ wherein one of the agents is epoxomicin, doxorubicin, DOXIL® [[doxil]], daunorubicin, idarubicin, epirubicin, aclarubicin, camptothecin, simvastatin, tannic acid, or cisplatin.

21. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents modulates subcellular localization of proteasomes.

22. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein the agent does not alter post-translational processing of ENaC.

23. (Currently Amended) The method of any one of claims 1 to 2 ~~or 10 to 12~~ wherein one of the agents modulates transcription of one or more molecules that regulate ENaC transcription.

24. (Withdrawn) The method of any one of claims 10 to 12 wherein the amount of agent decreases the level or amount of transcription for greater than one week.

25. (Withdrawn) The method of any one of claims 10 to 12 wherein the amount of agent decreases the level or amount of transcription for at least one day.

26. (Withdrawn) The method of any one of claims 10 to 12 wherein the amount of agent decreases the level or amount of transcription for at least 3 days.

27. (Withdrawn) The method of any one of claims 10 to 12 wherein the amount of agent decreases the level or amount of transcription for greater than two weeks.

28. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents modulates transport of molecules to or from the nucleus.

29. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is an endosomal protease inhibitor.

30. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is a cysteine protease inhibitor.

31. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents is not TPA.

32. (Withdrawn) The method of any one of claims 1 to 2 or 10 to 12 wherein one of the agents alters endosomal processing.

33. (Withdrawn) A method to inhibit or treat a condition associated with increased ENaC levels or increased ENaC activity, comprising: contacting a mammal at risk of or having the condition with an effective amount of an agent that inhibits or decreases transcription of one or more ENaC subunit genes and/or alters the level, amount or activity of a molecule that alters transcription of one or more ENaC subunit genes, and enhances the efficacy of gene therapy vectors.

34. (Withdrawn) A method to inhibit or treat a condition associated with increased ENaC levels or increased ENaC activity, comprising: contacting a mammal at risk of or having the condition with an effective amount of an agent that inhibits or decreases transcription of one or more ENaC subunit genes and/or alters the level, amount or activity of a molecule that alters transcription of one or more ENaC subunit genes, wherein the agent is a proteasome modulating agent, and wherein the agent is not a gene or gene product encoded by the genome of the mammal, the complement of the gene, or a portion of the gene or its complement.

35. (Withdrawn) A method to inhibit or treat a condition associated with increased ENaC levels or increased ENaC activity, comprising: contacting a mammal at risk of or having the condition with an effective amount of an agent that inhibits or decreases transcription of the α, β, and γ subunits of ENaC or alters the level, amount or activity of a molecule that alters transcription of the α, β, and γ subunits of ENaC.

36. (Withdrawn) A method to inhibit or treat a condition associated with increased ENaC levels or increased ENaC activity, comprising: contacting a mammal at risk of or having the condition with an effective amount of an agent that inhibits or decreases transcription of one or more ENaC subunit genes and/or alters the level, amount or activity of a molecule that alters transcription of one or more ENaC subunit genes, and enhances transduction of viruses which infect mammalian cells.

37. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is epoxomicin, doxorubicin, doxil, daunorubicin, epirubicin, idarubicin, aclarubicin camptothecin, simvastatin, tannic acid or cisplatin.

38. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is a chemotherapeutic.

39. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is an antibiotic.

40. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is a food additive.

41. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is a lipid lowering agent.

42. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent does not alter post-translational processing of ENaC.

43. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is not TPA.

44. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent modulates transcription of one or more molecules that modulate ENaC transcription.

45. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent modulates transport of molecules to or from the nucleus.

46. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent modulates subcellular localization of proteasomes.

47. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent decreases the level of ENaC transcription by at least 2 fold relative to a corresponding mammal not contacted with the agent.

48. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent decreases the level of ENaC transcription by at least 3 fold relative to a corresponding mammal not contacted with the agent.

49. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent decreases the level of ENaC transcription by at least 10 fold relative to a corresponding mammal not contacted with the agent.

50. (Withdrawn) The method of any one of claims 33 to 36 further comprising contacting the mammal with a recombinant virus.

51. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent is contacted with the respiratory tract of the mammal.

52. (Withdrawn) The method of any one of claims 33 to 36 wherein the agent enhances the efficacy or transduction of adenovirus, retrovirus, adeno-associated virus or lentivirus vectors.

53. (Withdrawn) The method of claim 33, 35 or 36 wherein the one agent is not a gene or gene product encoded by the genome of the cells, the complement of the gene, or a portion of the gene or its complement cells are mammalian kidney cells.